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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/585,925    06/02/00    RAFFERTY    P    2079.1024008

EXAMINER
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HM22/0524

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ART UNIT	PAPER NUMBER

1624

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*9*

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
09/585,925

Applicant(s)

Rafferty et al.

Examiner

Hong Liu

Art Unit

1624



-- The MAILING DATE of this communication appears on the cover sheet with the corresponding address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_\_
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-36 is/are pending in the application.
- 4a) Of the above, claim(s) 1-15 and 27-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16-26 and 36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirements.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5 & 7 20) ☐ Other:

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### **DETAILED ACTION**

Claims 1-36 are pending in this application.

#### ***Election/Restriction***

Applicants' election of Group VI subject matter along with species with traverse in Paper No. 8 is noted but is not found to be persuasive for the following reasons. The restriction requirement places the claims into groups of compound and methods of use. With regard to the separation of compound groups from method of use groups, MPEP. 806.05(h) permits restriction when more than one use can be shown exists for the compounds claimed. In the instant case uses such as treating hyperproliferative disorder, vascular hyperpermeability, angiogenesis, etc., as alleged by applicants are distinct uses irrespective of the mode(s) of action being relied on to treat the disorders. Note, compounds in the elected group also can be used for other uses such NMDA receptor antagonism, etc., as taught by Varano and other references, applied below. Different uses raise different issues of patentability over corresponding compound/composition claims. Note In re May 197 USPQ 601; In re Shetty 195 USPQ 753. Thus, the restriction is fully in compliance with the guideline of MPEP 806.05(f). In addition, as indicated in the previous office action, each of the groups belongs to a separate class and numerous subclasses. To search all the patents under these classes and subclasses would place a substantial burden on the examiner, let alone search of other non-patent literature.

For the above reasons, the restriction is still deemed proper and is therefore made FINAL.

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Claims 1-15 and 27-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 14, 15 and 28-33 should belong to Group I.

***Improper Markush Grouping***

Claims 16-26 and 36 are rejected under judicially created doctrine as being an improper Markush grouping. The recited compounds, while possessing a common utility, present a variable core and, thus, the Markush groups represented by the term where Y is O and Y is S have variably different definitions, render the claims clearly improper.

Deletion of non-elected subject matter would overcome this rejection.

***Claim Rejections - 35 USC § 112***

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 16-26 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making certain compounds wherein Q is CH, does not reasonably provide enablement for making compounds wherein Q is N. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

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3. The specification fails to enable the preparation of certain claimed compounds. According to the instant claims, in formula, ring A, R<sub>4</sub>, and R are defined to be “substituted or unsubstituted” Scope of “substituted and unsubstituted” in the claims read on all functional moieties regardless of complexity of structure. The nature of the invention in the instant application has claims which embrace a diversity of chemically and physically distinct compounds, wherein R or R<sub>4</sub> is an unsubstituted or substituted, single or fused, aromatic or an unsubstituted or substituted, fused or single, heteroaromatic group, containing one or more heteroatoms, etc. While many compounds are disclosed, there is insufficient guidance for preparing additional “protein kinase antagonists” which would be effective since the cited examples are drawn to a homogenous group of compounds not remotely commensurate in scope to applicants’ claims. Only compounds wherein R is pyrrole, indole, pyrrolo[2,3-b]pyridine have been made. From the schemes in the specification, it is clear that formulae VII and X (see page 63) are essential starting materials to prepare the claimed compounds. In the discussion of the sources of the starting materials in the examples, there is no disclosure regarding the compounds wherein Q is N needed to prepare the instantly claimed compounds. In view of the lack of direction provided in the specification regarding the starting materials and the general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in art to make the claimed compounds and therefore practice the invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- 1). "Substituted and unsubstituted" throughout claims 16-21 is unclear as to the nature and number of substituent(s) intended.
4. 2). The use of "heteroaryl" for R in claim 17 is unclear to the array of heteroatoms, size of the rings, as well as nature of atoms as ring members. See *In re Wiggins* 179 USPQ 421 for certain terminology regarding heterocyclic ring systems.
- 3). Claim 16 is vague and indefinite in that it recites the compounds "and physiologically acceptable salts..." It is not clear whether the claim is drawn to an instantly claimed compound or a mixture. The word "or" is suggested in place of "and".
- 4). Claim 16 is vague and indefinite in that the metes and bounds of "a substituent" for R<sub>2</sub> is unknown.
- 5). Where is "n" in the formula in claim 16?

***Claim Rejections - 35 USC § 102***

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 16 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Varano et al., Chem Abstract 131: 44782. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compound having RN 227012-80-8 and 227012-82-0.

Claims 16-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Gasprova et al., Chem Abstract 124: 55745. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds, i.e., R is heteroaryl.

Claims 16 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawashima et al. (WO 95/13269). Kawashima teaches the compounds and composition of the instant invention (see Example 7, page 20).

Claims 16 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawashima et al. (WO 94/05647). Kawashima teaches the compounds and composition of the instant invention (see Examples).

Claims 16 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Sakuta et al., Chem Abstract 119: 63033. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compound having RN 108402-28-4.

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Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by McCarthy et al., Chem Abstract 110: 38945. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds.

Claim 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Hamari et al., Chem Abstract 103: 142032. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds.

Claims 16 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Maki et al. (US Patent 4,490,292). Maki teaches the compounds and composition of the instant invention (see CAPLUS computer search report).

Claims 16 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Krapcho et al. (US Patent 4,078,062). Krapcho teaches the compounds and composition of the instant invention (see examples in the Table).

7. Claims 16 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Anzai et al., Chem Abstract 82: 140162. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compound having RN 54874-53-2, 54874-55-4, and 54874-62-3 wherein R is 2-furanyl, 54874-84-9, 54874-85-0.

Claims 16, 17, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Krapcho et al., (J. Med. Chem., 1973). The instantly claimed compounds read on the reference compound, see Table III, page 779.



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Claims 16 is rejected under 35 U.S.C. 102(b) as being anticipated by Shah et al., Chem Abstract 78: 124527. The instantly claimed compounds read on the reference compound, see the enclosed copy of CAPLUS computer search report and the compounds.

8. Claims 16 and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Gezgin et al. (Farmaco, 1997). Gezgin teaches the compounds and composition of the instant invention (see Table I).

### *Claim Rejections - 35 USC § 103*

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.


Claims 6 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krapcho et al. (US 4,078,062)). The reference teaches a generic group of compounds which embraces applicant's instantly claimed compounds. See formula I, Col. 1 wherein X can be hydrogen, halogen, lower alkyl, lower alkoxy, trifluoromethyl, amino, and nitro, R is hydrogen, etc. The compounds are taught to be useful as pharmaceutical agents. The claims differ from the reference by reciting a specific species and/or a more limited genus than the reference. However, it would have nevertheless been obvious to one skilled in the art at the time of the invention to be motivated to select any of the species of the genus taught by the reference including those

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instantly claimed, because the skilled chemist would have the reasonable expectation that any of the specie of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole. It has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within a genus. See *In re Susi*, 440 F.2d 442, 169 USPQ 423, 425 (CCPA 1971), followed by the Federal Circuit in *Merck & Co. V. Biocraft Laboratories*, 847 F.2d 804, 10 USPQ 2d 1843, 1846 (Fed. Cir. 1989).

Any inquiry concerning this communication should be directed to Examiner Hong Liu whose telephone number is (703) 306-5814. If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at (703) 308-4716. The fax phone number for this group is (703) 308-4734 for "unofficial" purposes and the actual number for **official** business is (703) 308-4556. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose number is (703) 308-1235.

hl  
May 21, 2001

  
**Mukund Shah**  
**Supervisory Patent Examiner**  
**Art Unit 1624**